UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/502,426	02/11/2000	Ricardo Azpiroz	2225-0001	5144

7590 05/19/2003

Ling-Fong Chung
Director, Intellectual Property Ceres, Inc.
3007 Malibu Canyon Road
Malibu, CA 90265

EXAMINER	
MEHTA, ASHWIN D	
ART UNIT	PAPER NUMBER
1638	24

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/502,426	AZPIROZ ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *88 and 89* is/are allowed.

6)☒ Claim(s) *58-61,63-70,72-79,81-87 and 90-94* is/are rejected.

7)☒ Claim(s) *62,71 and 80* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner. However, note the attached PTO-948.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

1. The transmittal filed on 03 March 2003 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/502,426 is acceptable and a RCE has been established. An action on the RCE follows.

2. The objection to the specification for failing to identify all of the sequences in Figure 3 using sequence identifiers is withdrawn, in light of the amendment to the brief description of that figure.

3. The rejection of claims 7, 12, 14-17, 19, and 43-45 under 35 U.S.C. 112, 2nd paragraph, is withdrawn in light of their cancellation.

4. The rejection of claims 5, 6, 8-10, 12, 14-17, 19, 20-45 under 35 U.S.C. 112, 1st paragraph, are withdrawn, in light of their cancellation.

5. The rejection of claims 5-10, 12, 14-17, 19, 20-45 under 35 U.S.C. 112, 1st paragraph, is withdrawn, in light of their cancellation.

Drawings

6. Informal, substitute drawings for Figures 1, 3, 9, 10A-10G, and 12 have been received. Applicants are asked to re-submit Figure 8. Original Figures 8 and 9 appeared on the same drawing sheet. The presence of original Figure 9, which has been cancelled in light of substitute Figure 9, may cause problems when printing Figure 8, should the instant application be found allowable. For this reason, Applicants are asked to re-submit Figure 8. Also note the Draftsperson's comments on the accompanying Form 948.

Claim Objections

7. Claims 62, 71, and 80 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claim 90 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claim is broadly drawn towards any isolated polynucleotide comprising nucleotides 6111-6468 of SEQ ID NO: 1.

The specification indicates that a 3' UTR spans bases 6111-6468 of SEQ ID NO: 1 (page 24, lines 2-3). The specification also indicates that UTRs can have regulatory functions related to, for example, translation rate and mRNA stability (page 31, lines 29-31).

However, the specification does not support a specific and substantial utility for bases 6111-6468 of SEQ ID NO: 1. All the specification teaches about this sequence is that it is part of a 3' UTR of the DWF4 gene. The specification does not teach the regulatory function of bases 6111-6468 of SEQ ID NO: 1, and further basic research is required to make this determination. Note, because the claimed invention is not supported by a specific and substantial utility, credibility cannot be assessed. Neither the specification nor any art of record discloses or suggests any property or activity of the nucleotide sequence such that another non-asserted utility would be well established.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 91-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 91 and 92: the recitation "the exogenous polynucleotide" in both claims renders them indefinite. There is improper antecedent basis for this recitation in the claims and the claims from which they depend.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 58-61, 63-70, 72-79, 81-87, and 90-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any isolated polynucleotide comprising a nucleic acid encoding a polypeptide having greater than 43%, from 85% to 90%, from 90% to 95%, or from 95% to 98% identity to the amino acid sequence set forth in SEQ ID NO: 2, said polypeptide effective to catalyze the hydroxylation of campestanol or 6-oxocampestanol; or wherein said polynucleotide further comprises a control element operably linked to said nucleic acid; a transgenic plant containing said polynucleotide; any host cell comprising said exogenous polynucleotide; a method of producing a polypeptide, comprising the steps of providing and culturing said host cell; an isolated polynucleotide comprising nucleotides 2102-3202 of SEQ ID NO: 1, or 1-3202 of SEQ ID NO: 1, 6111-6468 of SEQ ID NO: 1.

The specification describes the isolation and sequencing of a genomic clone (SEQ ID NO: 1) encoding the Arabidopsis DWF4 polypeptide (SEQ ID NO: 2; page 48, line 16 to page 52, line 25). The specification indicates that the DWF4 polypeptide of SEQ ID NO: 2 is a cytochrome P450 monooxygenase (page 52, lines 27-29), and that it is most similar at the amino acid level to another Arabidopsis cytochrome p450, CPD, with which it shares 43% identity and 66% similarity (page 54, lines 18-27). The specification at page 30, lines 24-28, indicates that

the coding region begins at nucleotide position 1133 in SEQ ID NO: 1. Figure 2 describes the locations of exon, introns, 5' and 3' untranslated regions of the genomic clone, as well as the locations of four domains in DWF4 that are found in cytochrome P450 proteins. The specification at page 71, line 30 to page 72, line 10 indicates that a 1.1 kb region of the genomic clone upstream of the translation initiation start was used a the promoter fragment in DWF4-promoter::GUS constructs. The specification indicates that in brassinosteriod synthesis, there are at least 2 branched pathways leading to the end product, brassinolide. The specification at page 69, line 30 to page 70, line 7 indicates that the Arabidopsis DWF4 polypeptide is a 22α-hydroxylase that catalyzes the 22α-hydroxylation steps of the brassinolide (BL) biosynthetic pathways, and has as substrates campestanol and 6-oxocampestanol (Figure 1).

However, the specification does not describe polynucleotides encoding polypeptides that differ from SEQ ID NO: 2 and still retain its functional activity. The specification at page 54, line 27 to page 54, line 3 indicates that SEQ ID NO: 2 has four domains that are typical of cytochrome P450s. As these four domains are present in other cytochrome P450s that catalyze different reactions, the presence of these domains in proteins having more than 43% identity, from 85% to 90%, from 90% to 95%, or from 95% to 98% to SEQ ID NO: 2 is not an indication that it has the same enzymatic activity. The correlation of the other amino acid sequences of SEQ ID NO: 2 to its functional enzymatic activity are not described. The specification then does not correlate any other structures other polynucleotides that encode polypeptides having the functional activity of SEQ ID NO: 2. Also see Fiers vs. Sugarno, 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere

statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself".

Regarding claim 90: the specification indicates that bases 6111-6468 of SEQ ID NO: 1 forms part of a 3' UTR of the DWF4 gene (page 24, lines 2-3). However, the specification does describe the functional activity of this base sequence. The specification indicates that UTRs "can" have regulatory functions (page 31, lines 29-31). However, the function for bases 6111-6468 of SEQ ID NO: 1 is not described. Given the breadth of the claims and lack of guidance of the specification as discussed above, the specification fails to provide an adequate written description of the multitude of polynucleotide sequences encompassed by the claims.

11. Claims 58-61, 63-70, 72-79, 81-87, and 90-94 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding SEQ ID NO: 2, plant host cells, transgenic plants comprising a polynucleotide encoding SEQ ID NO: 2, method of making a transgenic plant comprising introducing into a plant a polynucleotide encoding SEQ ID NO: 2, and a method for producing a polypeptide in plant cell comprising providing a plant host cell comprising an introducing polynucleotide encoding SEQ ID NO: 2, does not reasonably provide enablement for polynucleotides that do not encode SEQ ID NO: 2, non-plant host cells, and isolated polynucleotides comprising bases 6111 to 6468 of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any isolated polynucleotide comprising a nucleic acid encoding a polypeptide having greater than 43%, from 85% to 90%, from 90% to 95%, or from 95% to 98% identity to the amino acid sequence set forth in SEQ ID NO: 2, said polypeptide effective to catalyze the hydroxylation of campestanol or 6-oxocampestanol; or wherein said polynucleotide further comprises a control element operably linked to said nucleic acid; a transgenic plant containing said polynucleotide; any host cell comprising said exogenous polynucleotide; a method of producing a polypeptide, comprising the steps of providing and culturing said host cell; an isolated polynucleotide comprising nucleotides 2102-3202 of SEQ ID NO: 1, or 1-3202 of SEQ ID NO: 1, 6111-6468 of SEQ ID NO: 1.

As discussed above, the specification teaches the isolation and sequence of a genomic clone (SEQ ID NO: 1) encoding the Arabidopsis DWF4 polypeptide (SEQ ID NO: 2), and that DWF4 is a cytochrome P450 monooxygenase that is a 22α-hydroxylase that catalyzes the two 22α-hydroxylation steps of the brassinolide (BL) biosynthetic pathways and has as substrates campestanol and 6-oxocampestanol. Also as discussed above, the specification teaches the start of the coding region in SEQ ID NO: 1, the locations of the introns and exons of SEQ ID NO: 1, and that a 1.1 kb region upstream of the translation start site comprises the promoter activity required for proper transcription of dwf4. The specification also teaches that mutant dwf4 Arabidopsis plants have a dwarf phenotype, with short, rounded leaves (page 56, lines 16-18), and showed a delay in the start of flowering (page 57, lines 21-29, Table 1). The short stature of dwf4 mutant plants was due to a defect in cell elongation, as opposed to cell division (page 58, lines 20-30), and grew slower in the dark (page 62, lines 2-4). The dwf4 mutant plants were capable of perceiving gibberellic acid but failed to respond to exogenously applied gibberellic

acid. The dwf4 mutant plant also responded to inhibitory effects of auxin, but was incapable of auxin-stimulated elongation (page 62, lines 3-30). Exogenous application of BL restored wild-type growth to the mutant plants (page 62, line 13-24). To determine the step of the BL biosynthetic pathway affected in the dwf4 mutant, the mutant plant was grown in medium supplemented with the different known pathway intermediates. 22α-hydroxylated steroids rescued the mutant. The plants have no other defect other than in 22α-hydroxylation (page 67, line 23 to page 69, line 22). The specification also teaches the construction of recombinant vectors comprising the DWF4 coding region operably linked to the CaMV 35S promoter, and that transgenic Arabidopsis plants overexpressing DWF4 were produced (page 71, line 30 to page 77, line 23). Compared to non-transformed plants, DWF4 overexpression in transgenic plants resulted in increased plant height, larger leaves, increased seed production, and an increase in the number of branches.

The specification does not teach any nucleotide sequences other than those encoding SEQ ID NO: 2 that encodes an enzyme that catalyzes the hydroxylation of campestanol and 6-oxocampestanol. The specification teaches that the protein that is most similar to DWF4 is another cytochrome P450, CPD, with which it shares 43% identity and 66% similarity (page 54, lines 18-27). CPD acts on different substrates than DWF4 in the BL pathway (page 14, lines 26-30, Figure 1). However, it is highly inaccurate to simply assume that all amino acid sequences that have greater than 43% amino acid identity with SEQ ID NO: 2 will also share its functional activity. As discussed above, the specification teaches that DWF4 comprises four domains that are present in cytochrome P450 proteins. All of these proteins do not have the same functional activity. The specification does not teach the significance of the other amino acid sequences of

DWF4 protein, and provide no guidance in how the sequence of SEQ ID NO: 1 or SEQ ID NO: 2 may be changed without altering the enzymatic activity of SEQ ID NO: 2 (other than differences due to genetic code degeneracy). In the absence of further guidance, it would require undue experimentation for one skilled in the art to determine all of the changes that can be sustained by SEQ ID NO: 2 without altering its ability to catalyze the hydroxylation of campestanol and 6-oxocampestanol. Also see In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 UPSQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Regarding claim 90: Specifically, since the invention of claim 90 is not supported by either specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The specification indicates that bases 6111-6468 of SEQ ID NO: 1 is part of a 3' UTR of the DWF4 gene (page 24, lines 2-3). However, the specification does describe the functional activity of this base sequence. The specification indicates that UTRs "can" have regulatory functions (page 31, lines 29-31). However, the regulatory function of bases 6111-6468 of SEQ ID NO: 1 is not taught. It is not clear how one skilled in the art would use these sequences in the absence of further guidance in its function. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Regarding claims 91 and 92: as discussed above, the specification teaches that DWF4 catalyzes certain steps in the brassinolide biosynthetic pathway in plants, and that the overexpression of DWF4 in plants results in increased height. However, as DWF4 is a plant protein, it is not clear how one skilled in the art would use it in non-plant cells (other than bacterial cells such as *Escherichia coli*, which are routinely used in the art to store or amplify nucleotide sequences of interest, or *Agrobacterium*, which are used in plant transformation). See Genentech, Inc. V. Novo Nordisk, A/S, *supra*. It is suggested that claims 91 and 92 be limited to plant and bacterial host cells. Given the breadth of the claims, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

12. Claims 58-94 are deemed free of the prior art. Choe et al. (Plant Cell, February 1998, Vol. 10, pages 231-244) teach the isolation and nucleotide sequence of instant SEQ ID NO: 1. However, a declaration submitted by the inventors of the instant application on 12 June 2002 indicates that the authors of Choe et al. that are not inventors of the instant application did not conceive the claimed subject matter. As evidence indicating that the other authors of Choe et al. consider themselves to be co-inventors of the instant invention is lacking, Applicants' declaration was sufficient to remove this publication as a prior art reference.

13. Claims 88 and 89 are allowed. Claims 62, 71, and 80 are objected. Claims 58-61, 63-70, 72-79, 81-87, and 90-94 are rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

May 8, 2003

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER